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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

AUG 18 2003

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**COMPLETE IF KNOWN**

Application Number	10/042,761
Filing Date	January 15, 2003
First Named Inventor	A.G. Daifotis
Group Art Unit	To be determined
Examiner Name	To be determined
Attorney Docket Number	20002YPCI

**U.S. PATENT DOCUMENTS**

Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code (if known)		
<i>DK</i>	1	5,270,365		Gertz et al.	12/14/1993
	2	5,366,965		Strein	11/22/1994
	3	4,761,406		Flora et al.	08/02/1988
	4	4,425,339		Pitchford	01/10/1984
	5	4,621,077		Rosini et al.	11/04/1986
	22	5,616,560		Geddes	04/01/1997
	23	5,780,455		Brenner et al.	07/14/1998
	24	5,773,429		Fuisz	06/30/1998
	27	5,488,041		Barbier et al.	01/30/1996
	28	4,980,171		Fels et al.	12/15/1990
	40	4,812,304		Anderson et al.	03/14/1989
	41	4,822,609		Flora	04/18/1989
	48	5,358,941		Bechard et al.	10/25/1994
	49	5,616,571		Daifotis et al.	04/01/1997
	50	5,853,759		Katdare et al.	12/29/1998
	51	5,804,570		Santora II et al.	09/08/1998
	58	5,583,122		Benedict et al.	12/10/1996
	59	5,622,721		Dansereau et al.	04/22/1997
	60	4,927,814		Gall et al.	05/22/1990
<i>✓</i>	63	5,994,329		Daifotis et al.	11/30/1999

**FOREIGN PATENT DOCUMENTS**

Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Office	Number	Kind Code (if known)		
<i>DK</i>	6		WO 95/30421		Goodship et al.	11/16/1995
	7		WO 96/17616		Gazard	06/13/1996
	8		WO 94/00129		Francis et al.	01/06/1994
	9		WO 94/00130		Hovancik et al.	01/06/1994
	10		WO 94/21242		D'Souza et al.	09/29/1994
	25		WO 95/28145		Shinoda et al.	10/26/1995
	26		EP 0 600 834 A1		Goodship et al.	08/06/1994
	37		EP 0 274 158		Ebetino et al.	07/13/1988
	38		WO 95/08331		Bechard	03/30/1995
<i>✓</i>	39		WO 95/28936		Yates	11/02/199

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*T. A. Owens*

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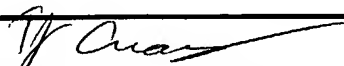
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## OTHER NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
<i>MC</i>	11	Lunar News, April 1997, "Update: Bisphosphonate", pp. 30-32
	12	Gertz et al., Osteoporosis Int. (1993), Suppl. 3: S13-16, "Clinical pharmacology of alendronate sodium"
	13	Gertz et al., Clin. Pharma. Ther. (1995), Vol. 58, pp. 288-98, "Studies of the oral bioavailability of alendronate"
	14	de Vernejoul et al., Calcified Tissue Int'l, Vol. 40 (1987), pp. 160-165, "Different schedules of administration of (3 amino-1-hydroxypropylidene)-1,1-bisphosphonate induce different changes ..."
	15	Lufkin et al., Osteoporosis Int'l. (1994), Vol. 4, pp. 320-322, "Pamidronate: An unrecognized problem in gastrointestinal tolerability".
	16	De Groen et al., N. England J. of Medicine, (1996), Vol. 335, pp. 1016-1021, "Esophagitis associated with the use of alendronate"
	17	Castell, (an editorial), N. England J. of Medicine (1996), Vol. 335, pp. 1058-1059, "Pill esophagitis - the case of alendronate".
	18	Liberman et al., (correspondence), N. England J. of Medicine (1996), Vol. 335, pp. 1069-1070, "Esophagitis and alendronate".
	19	Chesnut et al., Am. J. of Medicine, Vol. 99 (1995), pp. 144-152, "Alendronate treatment of the postmenopausal osteoporotic woman ...".
	20	Cassidy et al., Digestive Diseases and Sciences, Vol. 37 (1992), pp. 1206-1211, "Continuous versus intermittent acid exposure in production of esophagitis in feline model".
	21	Mortensen et al., J. of Bone & Mineral Res., (1995) Vol. 10, suppl. 1, p. s140, "Prevention of early postmenopausal bone loss of risendronate".
	29	Singer et al., Advances in Endocrin. & Metab., Vol. 6 (1995), pp. 259-288, "Bisphosphonates in the treatment of disorders or mineral metabolism".
	30	Lieberman et al., N. Eng. J. of Medicine, Vol. 333 (1995), pp. 1437-1443, "Effect of oral alendronate on bone mineral density and the incidence of fractures in postmenopausal osteoporosis".
	31	Bankhurst et al., Arthritis and Rheumatism, Vol. 38, No. 9, Suppl. 1 (1995), S359, "Three-year treatment with alendronate prevents fractures in women with postmenopausal osteoporosis".
<i>✓</i>	32	Filipponi et al., J. of Bone & Min. Research, Vol. 10 (1995), pp. 697-703, "Cyclical clondronate is effective in preventing postmenopausal bone loss: A comparative study with transcutaneous hormone replacement therapy".

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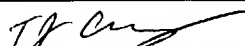
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Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
	33	McClung et al., Bone, Vol. 17 (1995), pp. 493S-496S, "Tiludronate therapy for Paget's disease of bone".
	34	Seltenmeyer et al., Bone (NY), Vol. 20, No. 4, Suppl., (1997) pp. 114S, "A comparison of the antiresorptive potency of various bisphosphonates in vivo with their inhibitory effect in vitro on squalene synthase and cellular sterol synthesis".
	35	Adachi et al., Today's Therapeutic Trends, Vol. 14, No. 1 (1996), pp. 13-24, "Osteoporosis -- its diagnosis, management and treatment with a new oral bisphosphonate agent, etidronate".
	36	Bell et al., Endocrine, Vol. 6(2) (1997), pp. 203-206, "Bisphosphonates in the Treatment of Osteoporosis".
	42	Melsen et al., Osteoporosis, Chapt. 60(1996), pp. 1145-1158, "ADFR - The Concept and its performance".
	43	Thompson et al., J. of Bone & Min. Research, Vol. 7(1992), pp. 951-960, "The bisphosphonate, alendronate, prevents bone loss in ovariectomized baboons".
	44	Balena et al., J. Clin. Invest., Vol. 92 (1993), pp. 2577-2586, "The effects of 2-year treatment with the aminobisphosphonate alendronate on bone metabolism, bone histomorphometry, and bone strength in ovariectomized nonhuman primates".
	45	Peter et al., Digestive Diseases & Sciences, Vol. 43 (1998), pp. 1009-1015, "Comparative study of potential for bisphosphonates to damage gastric mucosa of rats".
	46	Peter et al., Digestive Diseases & Sciences, Vol. 43 (1998), pp. 1998-2002, "Esophageal irritation due to alendronate sodium tablets".
	47	Harris et al., J. of Clin. Endoc. & Metab., 76:1399-1406 (1993), "The effect of short term treatment with alendronate on vertebral density and biochemical markers of bone...".
	52	Khan et al., Bone, Vol. 20 (1997), pp. 263-271, "Alendronate in the treatment of Paget's disease of bone".
	53	Physician's Desk Reference, 51st ed. (1997), pp. 1703-1706, "Fosamax".
	54	Gertz et al., J. of Bone & Min. Res., Vol. 9 (1994), pp 135-142, "Monitoring bone resorption in early postmenopausal women by an immunoassay for cross-linked collagen peptides in urine".
	55	Fleisch, J. of Clin. Endoc. & Metab., Vol. 76 (1993), pp. 1397-1398, "Editorial: Prospective use of bisphosphonates in osteoporosis".
	56	Chesnut et al., Osteoporosis Int'l (1993), Suppl. 3: S17-19, "Short-term effect of alendronate on bone mass and bone remodeling in postmenopausal women".

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Examiner Name	To be determined
Attorney Docket Number	20002YPCI

Sheet	5	of	8
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## OTHER NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
JK	57	Gertz et al., J. of Bone & Min. Res., Vol. 6, Suppl. 1 (1991), Abstract No. 790, p. S281, "Oral bioavailability and dose proportionality of alendronate (aminohydroxybutylidene bisphosphonate) in postmenopausal women".
	61	Mortensen et al., J. Bone & Min. Res., (1995), 10 (Supp. 1): S360, "Prevention of early postmenopausal bone loss by residronate: A two year study".
	62	Actonel™ (risedronate sodium tablets) package insert, dated March 1998.
	68	Lunar News (July 1996), "Update: Bisphosphonate", pp. 23-24
	69	Lunar News (April 1996), "Update: Bisphosphonate", p. 31
	70	The Pink Sheet (Dec. 18, 1995), Vol. 57, Issue 51, "Merck Cozaar generating 25,000 scripts weekly after six months on market; Foxamax off to quick start, company tells securities analyst meeting".
	71	Scrip (11/24/99), "Merck develops once-weekly Fosamax".
	72	Baran, Geriatrics, Vol. 56, No. 3 (March 2001), pp. 28-32, "Osteoporosis: Efficacy and safety of a bisphosphonate dosed once weekly".
	73	Bone et al., Clinical Therapeutics, Vol. 22, No. 1 (2000), pp. 15-28, "Weekly administration of alendronate: Rationale and plan for clinical assessment".
	74	Fleisch, Expert Opinion Therapeutic Patents, Vol. 11, No. 9 (2000), p. 1371-1381, "Bisphosphonates: mechanisms of action".
	75	Peter et al., Journal of Pharmacology & Experimental Therapeutics, Vol. 276, No. 1 (1996), p. 271-276, "Long-term safety of the aminobisphosphonate alendronate in adult dogs".
	76	Rodan et al., Osteoporosis International (1993) Suppl., 3:S7-12, "Preclinical Pharmacology of alendronate".
	77	Schnitzer, Expert Opinion Pharmacother., Vol. 2, No. 9 (2001), pp. 1461-1472, "Update on alendronate for osteoporosis: once-weekly dosing".
	78	Schnitzer et al., Aging: Clinical and Experimental Research, Vol. 12, No. 1 (2000), P. 1-12, "Therapeutic equivalence of alendronate 70 mg once-weekly and alendronate 10 mg daily in the treatment of osteoporosis".
✓	79	Seedor et al., Journal of Bone & Mineral Research, Vol. 6, No. 4 (1991), pp. 339-346, "The bisphosphonate alendronate (MK-217) inhibits bone loss due to ovariectomy in rats".

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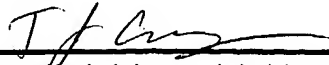
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## OTHER NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author, title, date, page(s), volume-issue number(s) and place of publication.
T/K	80	Sorrentino, Endoscopy, Vol. 28 (1996), p. 529, "Esophageal ulceration due to alendronate".
<del>T/K</del>	81	Blank, American College of Gastroenterology 66th Annual Scientific Meeting, "Lack of gastric adaptation to weekly versus daily alendronate administration in rats". <i>NO DATE</i>
T/K	82	Bone et al., Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), M392, "Once-weekly alendronate: Two year subgroup efficacy analyses in postmenopausal women with osteoporosis".
	83	Bone III et al., 6th International Symposium on Clinical Disorders of Bone and Mineral Metabolism, Venice, Italy, November 20-25, 1999, "Alendronate 70 mg once weekly is therapeutically equivalent to alendronate in 10 mg daily".
	84	Brown et al., Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), M402, "Efficacy, safety and tolerability of once weekly (80 mg vs. 160 mg) oral alendronate in postmenopausal osteoporosis".
	85	Delaney et al., ENDO 2001, The Endocrine Society's 83rd Annual Meeting, Denver, Colorado (June 2001), Abstract, P1-469 (June 2001), p. 249, "Bone density changes in response to risedronate once weekly".
	86	Gordon et al., ENDO 2001, The Endocrine Society's 83rd Annual Meeting, Denver, Colorado (June 2001), Abstract, P1-460 (June 2001), p. 247, "Weekly administration of risedronate increase bone mineral density".
	87	Lindsay et al., Arthritis & Rheumatism, Vol. 44, No. 9 (Suppl.), Abstract No. 604, "Risedronate 35 mg once a week is as effective as 5 mg daily in postmenopausal women".
	88	Rizzoli et al., Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), M401, "Two year results of once-weekly administration of alendronate 70 mg for the treatment of postmenopausal osteoporosis".
	89	Rizzoli et al., Annals of the Rheumatic Diseases, Annual European Congress of Rheumatology, EULAR 2001, Prague, Czech Republic, Vol. 60, Suppl. 1 (July 2001), Abstract SAT0164, p. 256, "Two year results of once-weekly administration of alendronate 70 mg for the treatment of postmenopausal osteoporosis".
	90	Van Dyke, et al., Annals of the Rheumatic Diseases, Annual European Congress of Rheumatology, EULAR 2001, Prague, Czech Republic, Vol. 60, Suppl. 1 (July 2001), Abstract SAT0167, p. 256, "Safety of once-weekly alendronate 70 mg in periodontal disease".
	91	Wimalawansa, Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), Abstract SA352, "Once a week alendronate therapy: A convenient and effective way of prevention and treatment of osteoporosis: A four-year clinical study".
	92	Wimalawansa, Journal of Bone & Mineral Research, Vol. 16, Suppl. 1 (September 2001), Abstract SU399, "Efficacy of once a week risedronate in comparison with once-weekly alendronate therapy for postmenopausal osteoporosis: One-year data".
	93	Wimalawansa, ENDO 2001, The Endocrine Society's 83rd Annual Meeting, Denver, Colorado (June 2001), Abstract P1-438, p. 241-242, "Highly efficacious and cost-effective alendronate regimen for postmenopausal osteoporosis: A four-year clinical study".
✓	94	Woodson, Osteoporosis International, Vol. 11, Suppl. 2 (2000), Chicago, Illinois, p. S204, Abstract 550 (514), "Once weekly risedronate therapy".

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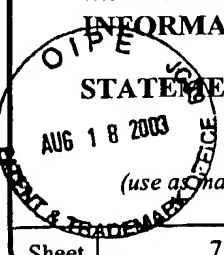
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	99	Men's Osteoporosis Support Group, Vol. 1, Issue 2, 1 July 1997
	100	Rote List 1997, 66 023 (Fosamax)
	101	Reddy M.S. et al, J. Periodontol, 1995, Vol. 66(3), pp. 211-217, "Alendronate Treatment of Naturally-Occurring Periodontitis in Beagle Dogs".
	102	Fleisch H., "Bisphosphonates in Bone Disease from the Laboratory to the patient", 1995 (Book)
	103	Black D.M. et al., The Lancet, 1996, 348, pp. 1535-1541, "Randomised trial of effect of alendronate on risk of fracture in women with existing vertebral fractures".
	104	Affidavit of Gideon Rodan from validity trial of IL 94612 dated 17 Nov. 2000
	105	Merck & Co., Inc. - Instructions for Once Weekly Fosamax, January 2001
	106	Lombardi et al., Ann. Ital. Med. Int. 7, 1992, 3 Suppl., pp. 158-165, "Clinical trials with bisphosphonates"
	108	Reid et al, American Journal of Medicine, 1996, Vol. 101, pp. 341-348, "Biochemical and Radiologic Improvement in Paget's Disease of Bone Treated with Alendronate: A Randomized, Placebo-controlled Trial".
	109	Passeri et al, Bone and Mineral, 1991, Vol. 15, pp. 237-248, "Intermittent treatment with intravenous 4-amino-1-hydroxybutylidene-1,1-bisphosphonate (AHBuBP) in the therapy of postmenopausal osteoporosis".
	110	Devogelaer et al, Bone, 1996, Vol. 18(2), pp. 141-150, "Oral Alendronate Induces Progressive Increases in Bone Mass of the Spine, Hip, and Total Body Over 3 Years in Postmenopausal Women with Osteoporosis".
	111	Siris et al, J. Clin. Endo. Metab., 1996, Vol. 81(3), pp. 961-967, "Comparative Study of Alendronate Versus Etidronate for the Treatment of Paget's Disease of Bone".
	112	Toolan et al, J. Bone Min. Res., 1992, Vol. 3, pp. 1399-1406, "Effects of 4-Amino-1-Hydroxybutylidene Bisphosphonate on Bone Biomechanics in Rats".
	113	Balena et al, Bone, 1993, Vol. 14, pp. 499-504, "the Aminobisphosphonate Alendronate Inhibits Bone Loss Induced by Thyroid Hormone in the Rat Comparison Between Effects on Tibiae and Vertebrae".
	114	Fleisch et al, Hormone and Metabolic Research, Vol. 29 (1997), pp. 145-150, "Bisphosphonates: Mechanisms of Action and Clinical Use in Osteoporosis - An Update".

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